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Cardiac Arrhythmias on 24-h Ambulatory Electrocardiography in Older Women and Men: The Cardiovascular Health Study

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Objectives. **This study describes the prevalence and correlates of cardiac arrhythmias in older persons.**

Background. **Cardiac arrhythmias are frequent in selected samples of elderly persons, but their prevalence and association with cardiovascular disease and its risk factors have not been examined in a large population-based sample.**

Methods. **In 1,372 participants in the Cardiovascular Health Study, a population-based study of cardiovascular disease risk factors, 24-h ambulatory electrocardiography was performed.**

Results. **Serious arrhythmias, such as sustained ventricular tachycardia and complete atrioventricular block, were uncommon, but brief episodes of ventricular tachycardia (≥3 consecutive ventricular depolarizations) were detected in 4.3% of women and 10.3% of men. Ventricular arrhythmias as a group (excluding ectopic beats <15/h) were more common in men than in women but were not significantly associated with age. The same patterns were true for bradycardia/conduction blocks. Supraventricular arrhythmias as a group (excluding ectopic beats <15/h), in contrast, did not differ by gender but were strongly associated with increased age. Multivariate analyses showed associations with arrhythmias to differ by gender, with only one association (increased age and supraventricular arrhythmias) present in both women and men. Ventricular arrhythmias, particularly in men, were associated with a higher prevalence of cardiovascular disease and its risk factors and with subclinical disease, as measured by increased left ventricular mass and impaired left ventricular function.**

Conclusions. **Arrhythmias are common in the elderly, and their association with cardiovascular disease differs by gender. Although risk related to arrhythmias can only be determined by prospective study, such studies should have adequate power to examine potential gender differences in associations.**

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Cardiac arrhythmias have been shown to be frequent in small samples of elderly persons undergoing ambulatory electrocardiographic (ECG) monitoring (1,2). Although arrhythmias often occur in the setting of underlying cardiovascular disease, in the absence of known disease or symptoms they have not been shown to be associated with increased mortality (3). Complex ectopic activity in the presence of normal coronary arteries has been associated with left ventricular diastolic enlargement (4,5), suggesting that ventricular arrhythmias may be markers of underlying or occult cardiovascular disease.

Although some studies have detected a relation of arrhythmias to cardiovascular disease risk factors, such as increased age (6), male gender (7), systolic hypertension (7), smoking (2) and cardiac enlargement (5,8), others have shown no relation at all between coronary risk status and arrhythmias on rest ECG (9). Many such studies have been small (7,9–11) and have included few subjects >65 years old (2,10,12). Subclinical or asymptomatic disease has not routinely been measured. These measures may be particularly important in the elderly, because cardiovascular disease is common and often unrecognized in these subjects (13,14).

The Cardiovascular Health Study (CHS) is a population-

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based longitudinal study of 5,201 adults aged ≥65 years that was designed to identify factors related to the onset and course of coronary disease and stroke. During the baseline CHS examination, 24-h ambulatory ECG monitoring was performed in a randomly selected subset of study participants. Baseline data were analyzed to 1) identify the frequency of arrhythmias in older men and women; 2) determine the associations between arrhythmias, cardiovascular and subclinical disease and cardiovascular disease risk factors; and 3) compare these relations in women and men.

Methods

Data collection. The CHS participants were recruited from a random sample of the Health Care Financing Administration Medicare eligibility lists in four U.S. communities: Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Pittsburgh (Allegheny County), Pennsylvania. Potential participants were excluded if they were institutionalized, wheelchair-bound in the home or currently under treatment for cancer. Details of the study design have been published elsewhere (15). Eligible participants gave informed consent and answered standard questionnaires on personal habits and medical history. Information on medication use in the preceding 2 weeks was collected from prescription bottles (16).

Participants were asked to fast for 12 h before their clinic visit. Sitting blood pressure was measured in the right arm after a 5-min rest. Duplicate measurements of supine blood pressure in both arms and both ankles were performed with a standard mercury sphygmomanometer and an 8-MHz Doppler probe. The ratio of these measures (the ankle-arm systolic blood pressure index) was used as a measure of arterial occlusive disease in the lower extremities (17). Blood pressure and heart rate were also measured in the supine position after a 30-min rest period and were repeated after 3 min of standing to assess postural changes.

Anthropometric measurements included weight and height in light clothing and no shoes. A 12-lead rest ECG and venipuncture were performed early in the clinic visit. Major and minor ECG abnormalities were defined by the Minnesota code (18). Multiple aliquots of plasma and serum were collected and shipped to a central laboratory for analyses of fasting lipids, coagulation factors and serum chemistry analyses.

Forced vital capacity and forced expiratory volume in 1 s were measured with a water-sealed spirometer. Carotid artery stenosis was defined by duplex ultrasonography interpreted by trained readers. Near- and far-wall maximal intimal-medial thicknesses of the carotid arteries were measured and averaged as an indicator of atherosclerosis. The CHS ultrasound methods and initial quality control results have been published elsewhere (19). M-mode echocardiography was used to measure dimensions of the left atrium and ventricle and thickness of the ventricular walls. Left ventricular mass was derived from the formula of Devereux et al. (20). Abnormalities of left ventricular ejection fraction, regional wall motion and left atrial chamber size were detected by inspection of two-dimensional echocardiographic images by trained readers and were classified on a qualitative basis as normal, borderline or abnormal. The borderline and abnormal classifications were combined into a single abnormal category for analysis. The CHS echocardiographic methods and initial quality control results have been published elsewhere (21).

Ambulatory ECG monitors were applied at the end of the clinical examination, usually between 11:00 AM and 1:00 PM, and were removed the following day. Five electrodes were applied to monitor two bipolar V_1- and V_5-like leads from the right subclavicular space to the V_5 position (lead CV_5) and from the left subclavicular space to the V_1 position (lead CV_1) using a Dynacord model 420 Cassette Holter Recorder (Del Mar Avionics). Recordings were analyzed for the presence and hourly frequency of arrhythmic events and ischemic episodes using Century model 48 hardware and software (Biomedical Systems) (22).

Ectopic beats were identified by creating templates of normally conducted QRS complexes and complexes considered to be ventricular ectopic complexes that were displayed to and classified by an operator whenever there was uncertainty in the computer algorithm. Supraventricular ectopic complexes were those with QRS morphology matching the template of normally conducted complexes and were detected strictly by their prematurity in the cardiac cycle. An approximate 5% sample of recordings was reprocessed at monthly intervals for quality control. Correlation coefficients of duplicate ventricular and supraventricular ectopic complex counts were 0.96 and 0.90, respectively.

Definitions. Prevalent myocardial infarction, angina pectoris, congestive heart failure, stroke, transient ischemic attack and peripheral vascular disease were defined as positive answers to the question, "Has a doctor ever told you that you had . . . ," confirmed by review of medical records (23). Subjects with major Q/QS waves (Minnesota codes 1.1.1 to 1.2.7 and 1.2.9 [18]) on rest ECG- or ankle-arm index <0.8 were also considered to have prevalent myocardial infarction and prevalent peripheral vascular disease, respectively. Coronary artery disease was considered to be reported and confirmed (or silent) myocardial infarction or reported and confirmed angina, or both.

Diabetes was defined as self-report of physician-diagnosed diabetes, current use of hypoglycemic medications, fasting glucose ≥140 mg/dl or 2-h postload glucose ≥200 mg/dl. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg or current use of antihypertensive medications. Obesity was defined as >20% above ideal body weight, as defined by the Metropolitan Life Insurance Company (24). ST segment depression was defined as ST segment ≥100 μV below the PR baseline and 24-h median ST segment sustained for at least 1 min (22). QT intervals were corrected for heart rate by calculating the QT index, equal to the measured QT

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Table 1. Prevalence of Specific Arrythmias by Gender* (in 729 Women and 643 Men)

	Women		Men		
	No.	%	No.	%	p Value
Ventricular arrhythmias	114	15.6	183	28.5	0.0001
Ventricular tachycardia >15 complexes	2	0.3	1	0.2	NS
Ventricular tachycardia ≥3 complexes	31	4.3	66	13	0.0001
Frequent ventricular ectopic beats (≥15/h)	100	13.7	160	24.9†	0.0001
Minor ventricular arrhythmias any ventricular ectopic beats	554	76.0	570	88.7	0.0001
Supraventricular arrhythmias	422	55.5	381	57.1	NS
Tachyarrhythmias/bradyarrhythmias	1	0.1	2	0.3	NS
Supraventricular tachycardia >15/h and rate >130/min	15	2.1	14	2.2	NS
Sustained atrial fibrillation or atrial flutter	12	1.7	16	2.5	NS
Intermittent atrial fibrillation or atrial flutter	8	1.1	5	0.8	NS
Frequent supraventricular ectopic beats (≥15/h)	132	18.1‡	186	28.2§	0.0001
Supraventricular tachycardia ≥3 complexes	364	49.9†	307	47.7§	NS
Minor supraventricular arrhythmias any supraventricular ectopic beats	708	97.1	625	97.2	NS
Bradycardias/conduction blocks	14	1.9	36	5.6	0.0001
Complete AV block	0	0.0	2	0.3	NS
Mobitz type II AV block	3	0.4	5	0.8	NS
Pause >3 s	3	0.4	4	0.6	NS
Bradycardia ≤40 beats/min	10	1.4	28	4.4	0.001

*Each subject can be in more than one category. †$p < 0.01$, patients with arrhythmia significantly older than those without. ‡$p < 0.005$, patients with arrhythmia significantly older than those without. §$p < 0.0005$, patients with arrhythmia significantly older than those without. AV = atrioventricular.

interval (ms) divided by {656/(1 + 0.01 × Heart rate)}. QT prolongation was defined as QT index >110, which was the upper 2.5 percentile limit established for a larger normal population sample <75 years old (25).

Ventricular arrhythmias as a group included ventricular tachycardia (≥3 consecutive complexes) and frequent ventricular ectopic activity (≥15 complexes/h). Supraventricular arrhythmias included tachyarrhythmias/bradyarrhythmias (heart rate ≤40 and ≥130 beats/min sustained >12 s), sustained or intermittent atrial fibrillation or flutter, frequent supraventricular ectopic activity (≥15 complexes/h) and supraventricular tachycardia (≥3 consecutive complexes). Bradycardia/conduction blocks included Mobitz type II or third-degree atrioventricular (AV) block, pauses >3 s and bradycardia ≤40 beats/min sustained >12 s.

Population included in analysis. Ambulatory ECGs were recorded in 1,512 subjects. Nine cassettes (0.6%) were blank on receipt at the Electrocardiographic Reading Center; 75 recordings (5%) were rejected because of excessive noise; and 56 (4%) were rejected for the duration of monitoring >18 h, leaving 1,372 subjects for analysis. The subsample of monitored participants was younger (mean age 71.9 vs. 73.1 years in those not monitored, $p < 0.0001$) and more likely to be male (47% vs. 42% not monitored, $p < 0.002$) but did not differ from the unmonitored group in prevalence of hypertension or coronary disease.

Statistical analysis. Bivariate associations with ambulatory ECG abnormalities were assessed by chi-square analysis and *t* tests for categoric and continuous variables, respectively. Comparisons of left ventricular mass and lung volumes were adjusted for body surface area and height, respectively, using analysis of covariance. Factors associated at $p < 0.05$ in bivariate analysis were entered into multiple logistic regression models using the grouped arrhythmia categories (ventricular, supraventricular and bradycardia/conduction blocks) as dependent variables, with age forced into each model. Body size variables were also forced into models that included body size-dependent factors, such as left ventricular mass or lung volumes. All analyses were stratified by gender, and multivariate models were repeated after excluding subjects with prevalent coronary artery disease. All analyses were performed using the Statistical Analysis System (SAS) (26).

Results

Prevalence and diurnal patterns of arrhythmias. Although prevalence of serious arrhythmias, such as sustained ventricular tachycardia and complete AV block, was quite low (Table 1), ventricular tachycardia (≥3 consecutive ventricular depolarizations) was detected in 4.3% of women and 10.3% of men. Supraventricular tachycardia (≥3 consecutive supraventricular depolarizations) was detected in nearly half of all subjects. Ventricular and supraventricular ectopic activity was extremely common. Only 18% and 2.8% of subjects were completely free of ventricular and supraventricular ectopic activity, respectively.

Men were more than three times as likely to have sustained bradycardia and more than twice as likely to have ventricular tachycardia ≥3 complexes as were women. Men also had excess prevalence of frequent (≥15/h) ventricular and supraventricular ectopic beats. Ventricular arrhythmias

Table 2. Prevalence of Arrhythmias by Age, Gender and Type of Arrhythmia

Age (yr)	Total No.	Ventricular Arrhythmias No.	%	Supraventricular Arrhythmias No.	%	Bradycardia/ Conduction Blocks No.	%
Women							
65–69	325	46	14	165	40	5	1.5
70–74	234	42	18	130	56	4	1.7
75–79	121	21	17	79	65	4	3.3
80+	49	5	10	37	76	1	2.0
Total	729	114	16	411	56	14	1.9
Men							
65–69	223	59	26	102	46	14	6.3
70–74	223	60	27	128	57	10	4.5
75–79	124	36	29	82	66	5	4.0
80+	73	28	38	57	78	7	9.6
Total	643	183	28	369	57	36	5.6
Gender difference		p = 0.0001		p = NS		p = 0.0001	
Age association							
Women		p = NS		p = 0.0001		p = NS	
Men		p = NS		p = 0.0001		p = NS	
Prevalence Excluding Coronary Artery Disease*							
Women	552	81	15	312	57	9	1.6
Men	378	93	25	218	58	23	6.1
Prevalence Excluding Coronary Artery Disease, Hypertension and Diabetes†							
Women	234	25	11	127	54	2	0.9
Men	158	32	20	100	63	8	5.1

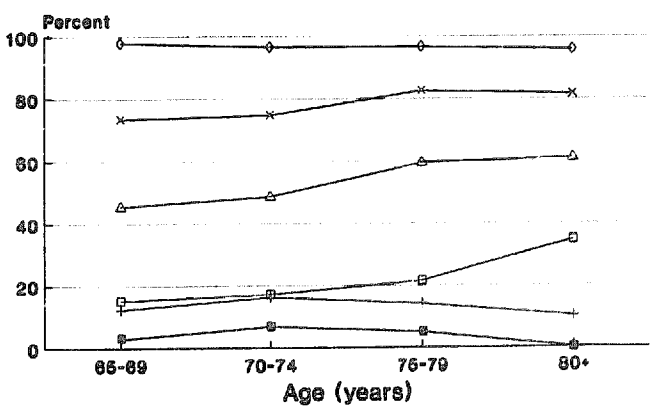
*Excluding subjects with previous coronary heart disease, abnormal echocardiographic left ventricular ejection fraction or wall motion, ST segment depression ≥60 s and carotid artery stenosis ≥50%. †Excluding subjects with previous coronary heart disease, abnormal echocardiographic left ventricular ejection fraction or wall motion, ST segment depression ≥60 s, carotid artery stenosis ≥50%, hypertension and diabetes.

as a group were more common in men than in women but were not significantly associated with age (although a trend was present toward older age in men with arrhythmias, $p < 0.06$). The same patterns were true for bradycardia/conduction blocks (Table 2). Supraventricular arrhythmias, in contrast, did not differ by gender but were strongly associated with increased age. Most of this increase was due to increases in frequent supraventricular ectopic beats and supraventricular tachycardia ≥3 beats with increasing age, especially in women (Fig. 1). Ventricular tachycardia ≥3 beats and frequent ventricular ectopic activity increased slightly and then declined in prevalence with increasing age in women, whereas in men, both increased steadily with age in these cross-sectional data (Fig. 2).

Exclusion of subjects with known clinical coronary artery disease or evidence of subclinical disease slightly reduced the prevalence of ventricular arrhythmias (from 16% to 15% in women and 28% to 25% in men) and bradycardia/conduction blocks. Further exclusion of subjects with hypertension or diabetes reduced the prevalence of ventricular arrhythmias by approximately one-third and bradycardia/conduction blocks in women by approximately one-half.

Correlation of arrhythmias with risk factors and disease. Associations of ventricular arrhythmias with prevalent and subclinical disease and risk factors are shown for women and

Figure 1. Frequency of ventricular and supraventricular ectopic activity by age in women: ventricular (solid squares) and supraventricular (triangles) tachycardia; ventricular (vertical bars) and supraventricular (open squares) ectopic activity (>15/h); any ventricular (crossmarks) and supraventricular (diamonds) ectopic activity.



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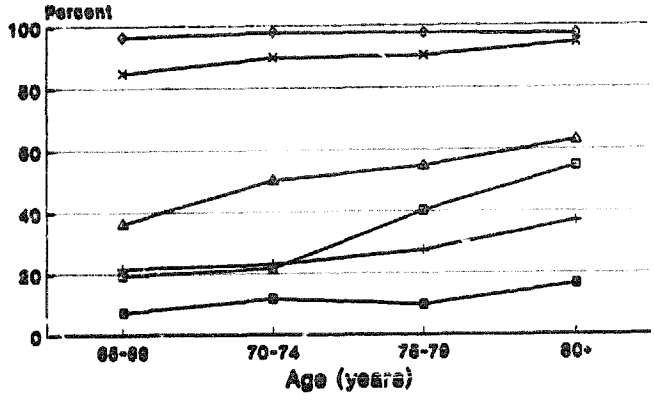

Figure 2. Frequency of ventricular and supraventricular ectopic activity by age in men. Symbols as in Figure 1.

men in Table 3. In women, ventricular arrhythmias were not associated with prevalent disease but were strongly related to increased left ventricular internal diastolic dimension, a measure of subclinical disease. They were less strongly associated with other subclinical measures in women, such as increased left ventricular mass and carotid artery wall thickness, and with diminished lung volumes. Medication use, particularly diuretic agents, was also strongly associated with ventricular arrhythmias in women. In men, ventricular arrhythmias were strongly associated with prevalent disease and measures of subclinical disease, such as abnormal left ventricular ejection fraction, increased left ventricular internal dimension, increased echocardiographic left ventricular mass and diminished lung volumes. Weaker relations were seen with low ankle-arm index, use of antihypertensive medications and carotid artery wall thicknesses in men.

Fewer associations were detected for supraventricular arrhythmias (Table 4). In women, these arrhythmias were strongly related to leanness, digitalis use, maximal common carotid artery thickness and lung volumes. None of the associations significant in women were significant in men, and vice versa, although many tended in the same direction. Supraventricular arrhythmias in men were strongly related to beta-adrenergic blocking agent use, height and echocardiographic left ventricular mass.

Bradycardia/conduction blocks demonstrated still fewer associations, and, again, these differed by gender (Table 5). In women, these arrhythmias were strongly related to antihypertensive drug use, transient ST segment depression, major ST-T wave abnormalities and Factor VII activity and in men to diastolic pressure, fibrinogen and increased ECG left ventricular mass. The only relation with bradycardia/conduction blocks common to men and women was with lower fasting insulin levels. Bivariate associations with subclinical disease, risk factors and symptoms were essentially unchanged after excluding 275 subjects with known coronary artery disease (data not shown).

Multiple logistic regression of arrhythmia classes stratified by gender showed a distinct segregation of risk factors between men and women (Table 6). Associations between ventricular arrhythmias and abnormal left ventricular ejection fraction, forced vital capacity and height were limited to men in these multivariate models, whereas diuretic agent use and prolonged QT intervals were limited to women. Associations between supraventricular arrhythmias and abnormal left atrial chamber size and digitalis use were limited to women, whereas beta-blocker use and transient ST segment depression were limited to men. Antihypertensive drug use, fibrinogen and Factor VII were associated with bradycardia/conduction blocks in women, and diastolic pressure, fibrinogen and ECG left ventricular mass were independently associated only in men. After adjusting for these factors, insulin levels were not associated with bradycardia/conduction blocks in women or men.

Discussion

Prevalence of arrhythmias was similar in this study to that documented in other samples of elderly subjects (1,2,10,27). In contrast to other reports (2,10,28–30), a substantial gender difference was evident in prevalence of ventricular arrhythmias and bradycardia/conduction blocks. These differences remained after excluding subjects with known cardiovascular disease. Failure to find such associations in other studies may have been due to the small number of women studied or to small overall sample size.

Strengths of the current study include its large size and population-based sampling method, although minor biases were detected in subjects undergoing Holter monitoring. Although men were slightly overrepresented in the Holter subsample compared with the overall CHS sample, the proportion of women was still far in excess of previously reported studies. The slightly younger age of the Holter subsample may reflect this gender difference and might be expected to lead to underestimation of arrhythmia prevalence if generalized to the entire CHS sample.

Gender differences in multivariate associations with arrhythmias. The marked discordance in multivariate associations with arrhythmias by gender was not expected and has not to our knowledge been previously reported. Although bivariate analysis showed many associations to have similar trends in women and men, this was not true of the multivariate models. One might expect such differences to arise if factors measuring similar conditions and having similar relations to arrhythmias differed in prevalence or measurement accuracy by gender, thus affecting statistical power. Such might conceivably be the case for fibrinogen and Factor VII, for example, or for diastolic pressure or antihypertensive agent use. It is difficult to argue, however, that prolonged QT interval and diuretic agent use in women are in any way similar to forced vital capacity and height in men. Similarly, how could abnormal left atrial size and digitalis use in women be measured against beta-blocker use and transient ST segment depression in men?

Table 3. Associations of Ventricular Arrhythmias With Clinical and Subclinical Disease and Risk Factors in Women and Men*

Prevalence of Ventricular Arrhythmias in Presence of Various Conditions						
	Women			Men		
	Total No.	No. (%)	p Value	Total No.	No. (%)	p Value
Myocardial infarction						
Present	50	7 (14)	NS	120	50 (42)	0.0001
Absent	679	107 (16)		523	133 (25)	
Coronary artery disease						
Present	102	14 (14)	NS	173	63 (36)	0.007
Absent	627	100 (16)		470	120 (26)	
Major Q/QS waves						
Present	23	2 (8.7)	NS	52	23 (44)	0.009
Absent	706	112 (16)		591	160 (27)	
Ankle-arm index						
<0.9	47	9 (19)	NS	81	31 (38)	0.04
≥0.9	664	102 (15)		556	150 (27)	
LV ejection fraction						
Abnormal	27	7 (26)	NS	94	40 (43)	0.001
Normal	692	104 (15)		547	142 (26)	
LV regional wall motion						
Abnormal	31	8 (26)	NS	98	38 (39)	0.02
Normal	687	104 (15)		543	144 (27)	
Prolonged QT interval						
Present	124	27 (22)	0.04	86	33 (38)	NS
Absent	605	87 (14)		557	150 (27)	
Diuretic agent use						
Present	211	45 (21)	0.006	147	53 (36)	0.02
Absent	517	68 (13)		496	130 (26)	
Beta-blocker use						
Present	86	21 (24)	0.02	104	34 (33)	NS
Absent	642	92 (14)		539	149 (28)	
Antihypertensive agent use						
Present	323	61 (19)	0.03	282	94 (33)	0.02
Absent	405	52 (13)		261	89 (25)	

Mean Levels of Various Factors in Presence of Ventricular Arrhythmias						
	Women			Men		
	Arrhythmia			Arrhythmia		
	Present	Absent	p Value	Present	Absent	p Value
LV internal diastolic dimension (cm)	5.00	4.71	0.0001	5.45	5.20	0.002
Mean echo LV mass (g)†	140	131	0.03	194	171	0.0001
Mean ECG LV mass (g)†	173	167	0.05	232	219	0.02
Mean common carotid artery wall thickness (mm)	0.86	0.82	0.01	0.93	0.90	NS
Maximal common carotid artery wall thickness (mm)	0.99	0.95	0.03	1.09	1.04	0.03
Maximal internal carotid artery wall thickness (mm)	1.38	1.33	NS	1.71	1.58	0.03
Mean FEV_1 (liters)‡	1.80	1.90	0.03	2.37	2.53	0.003
Mean FVC (liters)‡	2.49	2.60	0.04	3.48	3.70	0.0005
Weight (kg)	70.1	67.6	NS	81.4	79.2	0.04

*Only associations significant in women or men are shown. Factors examined for associations with arrhythmias included previous infarction, angina, coronary heart disease, congestive heart failure, stroke/transient ischemic attack, peripheral vascular disease, abnormal left ventricular (LV) ejection fraction, abnormal left ventricular regional wall motion, left atrial dimension, echocardiographic (echo) left ventricular mass, electrocardiographic (ECG) left ventricular mass, forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), ≥50% carotid artery stenosis, mean and maximal common carotid artery far wall thickness, mean and maximal internal carotid artery far wall thickness, ankle-arm index, ST segment depression ≥60 s, hypertension, systolic or diastolic blood pressure, diabetes, cigarette smoking, alcohol use, obesity, total cholesterol, high density lipoprotein cholesterol, insulin, potassium, creatinine, fibrinogen, Factor VII, orthostatic hypotension, ventricular conductive defects, major Q/QS waves, major ST-T wave abnormalities, prolonged QT interval, spinning sensation, loss of balance, blackouts or fainting, frequent falls, palpitations, dizziness on standing, current dizziness or use of digitalis or diuretic, beta-adrenergic blocking or antihypertensive agents. †Adjusted for body surface area. ‡Adjusted for height.

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Table 4. Associations of Supraventricular Arrhythmias With Clinical and Subclinical Disease and Risk Factors in Women and Men*

	Prevalence of Supraventricular Arrhythmias in Presence of Various Conditions					
	Women			Men		
	Total No.	No. (%)	p Value	Total No.	No. (%)	p Value
LA chamber size						
Abnormal	114	76 (67)	0.02	131	84 (64)	NS
Normal	609	331 (54)		508	284 (56)	
ST segment depression ≥60 s						
Present	59	38 (64)	NS	79	55 (70)	0.02
Absent	670	373 (56)		564	314 (56)	
Major ST-T wave abnormalities						
Present	49	36 (73)	0.02	32	19 (59)	NS
Absent	680	375 (55)		611	350 (57)	
Obesity						
Present	291	225 (51)	0.001	265	142 (54)	NS
Absent	438	186 (64)		378	227 (60)	
Cholesterol						
≥240 mg/dl	252	136 (54)	NS	98	46 (47)	0.03
<240 mg/dl	477	275 (58)		545	323 (59)	
Digitalis use						
Present	48	40 (83)	0.0001	59	38 (64)	NS
Absent	680	370 (54)		584	331 (57)	
Beta-blocker use						
Present	86	45 (52)	NS	104	46 (44)	0.003
Absent	642	365 (57)		539	323 (60)	
	Mean Levels of Various Factors in Presence of Supraventricular Arrhythmias					
	Women			Men		
	Arrhythmia			Arrhythmia		
	Present	Absent	p Value	Present	Absent	p Value
Total cholesterol (mg/dl)	223	225	NS	200	206	0.04
Height (cm)	159	159	NS	174	172	0.005
Mean echo LV mass (g)†	135	129	NS	184	167	0.002
Mean ECG LV mass (g)†	170	164	0.02	226	216	NS
Mean common carotid artery wall thickness (mm)	0.84	0.80	0.01	0.91	0.91	NS
Maximal common carotid artery wall thickness (mm)	0.97	0.93	0.005	1.06	1.06	NS
Mean FEV_1 (liters)‡	1.83	1.95	0.0004	2.44	2.54	NS
Mean FVC (liters)‡	2.52	2.66	0.0003	3.61	3.67	NS
Weight (kg)	67.0	69.2	0.02	79.3	80.4	NS

*Only associations significant in women or men are shown (see Table 3 for complete listing of associations examined). †Adjusted for body surface area. ‡Adjusted for height. LA = left atrial; other abbreviations as in Table 3.

Few studies have examined ventricular arrhythmias in women, and except for one study of female medical students (31), they have almost exclusively dealt with subjects with known heart disease. Moss et al. (32) reported an interesting lack of association in women between ventricular arrhythmias and mortality 2 years after discharge for myocardial infarction. They postulated that womens' smaller hearts or lower rates of cigarette smoking might have put them at lower risk for ventricular arrhythmias but were unable to evaluate these hypotheses with the available data. Correlates of arrhythmias in women were not presented. No other studies to our knowledge have examined correlates of arrhythmias specifically in women, although female survivors of cardiac arrest have been reported to be less frequently inducible on electrophysiologic testing than male survivors (33). Whether the differences in associations observed in the current study reflect a survival bias among women, a lack of statistical power because of smaller sample sizes or actual biologic differences in arrhythmias by gender cannot be determined at present. Follow-up of this cohort to determine risk of arrhythmias and examination of other cohorts to determine gender-specific associations with arrhythmias are needed to evaluate this finding properly.

Relation to subclinical disease. Presence and severity of ventricular arrhythmias have been shown to be independent predictors of mortality in survivors of myocardial infarction (34–36) and to be associated with severity of left ventricular dysfunction after infarction (4,37). Ventricular arrhythmias

Table 5. Associations of Bradycardia/Conduction Blocks With Clinical and Subclinical Disease and Risk Factors in Women and Men*

Prevalence of Bradycardia/Conduction Blocks in Presence of Various Conditions						
	Women			Men		
	Total No.	No. (%)	p Value	Total No.	No. (%)	p Value
Major ST-T wave abnormalities						
Present	49	4 (8.2)	0.001	32	0 (0.0)	NS
Absent	680	10 (1.5)		611	36 (5.9)	
ST segment depression ≥60 s						
Present	59	4 (6.8)	0.005	79	3 (3.8)	NS
Absent	670	10 (1.5)		564	33 (5.9)	
Digitalis use						
Present	48	3 (6.3)	0.03	59	6 (10.0)	NS
Absent	680	11 (1.6)		584	30 (5.1)	
Antihypertensive agent use						
Present	323	13 (3.7)	0.002	282	16 (5.7)	NS
Absent	405	2 (0.5)		261	20 (5.5)	

Mean Levels of Various Factors in Presence of Bradycardia/Conduction Blocks						
	Women			Men		
	Arrhythmia			Arrhythmia		
	Present	Absent	p Value	Present	Absent	p Value
Diastolic blood pressure (mm Hg)	69	63	NS	67	73	0.03
Mean ECG LV mass (g)†	169	168	NS	254	220	0.002
Fasting insulin (μU/dl)	12	18	0.0001	12	19	0.0001
Fibrinogen (mg/dl)	290	320	NS	292	318	0.006
Factor VII (% activity)	112	136	0.0002	109	114	NS

*Only associations significant in women or men are shown (see Table 3 for complete listing of associations examined). †Adjusted for body surface area. Abbreviations as in Table 3.

have also been shown to be associated with a fourfold increased risk of developing overt ischemic heart disease (38).

Prospective studies have failed to show an association between ventricular arrhythmias and risk of sudden or coronary death or total mortality in healthy, asymptomatic subjects (1,3,11,29,39,40). These studies have frequently been conducted in small samples, however, and have not included sensitive measures of subclinical cardiovascular disease. Those that have included such measures have shown an increased frequency of ventricular enlargement even among asymptomatic subjects with complex ventricular ectopy (5,8).

Participants in the current study with a qualitatively abnormal left ventricular ejection fraction had a 1.7-fold increased prevalence of ventricular arrhythmias on bivariate analysis. Similarly, qualitatively abnormal left ventricular regional wall motion was associated with a 1.4- to 1.7-fold increased prevalence of arrhythmias. The lack of significance of the association with abnormal ejection fraction in women, despite a prevalence ratio similar to men, is most likely due to the small number of women (n = 27) with this abnormality. Men with an abnormal left ventricular ejection fraction had twice the prevalence of ventricular arrhythmias after adjustment for other factors, such as age and forced vital capacity. The persistence of these associations after exclusion of subjects with prevalent coronary artery disease suggests that subjects with ventricular arrhythmias are more likely to have subclinical disease than those without arrhythmias. Still, the vast majority of subjects with arrhythmias did not have these abnormalities, suggesting that arrhythmias have a low predictive value for subclinical disease in a population-based sample.

After excluding participants with known cardiovascular disease, associations with these subclinical measures were essentially unchanged, suggesting that noninvasive abnormalities are associated with ventricular arrhythmias in elderly subjects regardless of the presence of known cardiovascular disease. The strong associations of ventricular arrhythmias with measured left ventricular mass, abnormal left ventricular ejection fraction and carotid artery wall thickness, even in subjects without cardiovascular disease, suggest that these arrhythmias are linked to cardiovascular disease that may be occult or subclinical. This may be particularly true in the elderly, who have a high prevalence of unrecognized or asymptomatic disease (13,14).

Relation to cardiovascular disease risk factors. Because subjects with overt cardiovascular disease are more likely to have risk factors for the disease or to have had them at some time in the past, one might suspect that associations between

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Table 6. Multiple Logistic Regression Models of Arrhythmias, Stratified by Gender

	Women		Men	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Ventricular arrhythmias				
Age (7 yr)*	1.10	(0.90, 1.35)	1.26	(0.98, 1.62)
Abnormal LV ejection fraction	—	—	2.05	(1.25, 3.37)
Prolonged QT interval	1.77	(1.10, 2.85)	—	—
Diuretic agent use	1.84	(1.17, 2.88)	—	—
FVC (1.1 liters)	—	—	0.63	(0.47, 0.85)
Height (14 cm)	—	—	2.15	(1.38, 3.33)
Supraventricular arrhythmias				
Age (7 yr)	1.53	(1.20, 1.95)	1.77	(1.39, 2.25)
Abnormal LA chamber size	3.61	(1.47, 8.86)	—	—
Digitalis use	3.02	(1.35, 6.74)	—	—
Beta-blocker use	—	—	0.57	(0.36, 0.88)
Transient ST segment depression	—	—	1.73	(1.01, 2.94)
Conduction blocks/bradycardia				
Age (7 yr)	1.36	(0.61, 3.03)	0.97	(0.61, 1.56)
Antihypertensive agent use	8.31	(1.79, 38.5)	—	—
Diastolic pressure (mm Hg)	—	—	0.57	(0.35, 0.94)
Fibrinogen (77 mg/dl)	0.41	(0.18, 0.96)	0.57	(0.35, 0.93)
Factor VII (36% activity)	0.35	(0.15, 0.79)	—	—
ECG LV mass (54.4 g)†	—	—	1.39	(1.10, 1.75)

*Numbers in parentheses represent interquartile range for each variable (75th to 25th percentile), which is multiplied by a beta-coefficient and exponentiated to an estimate of the odds ratio. Variables without ranges are dichotomous, and the odds ratio represents the estimated risk associated with the presence of that factor. †Body surface area forced into models with electrocardiographic (ECG) left ventricular (LV) mass was not significant and did not change associations. CI = confidence interval; FVC = forced vital capacity; LA = left atrial.

arrhythmias and risk factors reflect the presence of cardiovascular disease. In these older subjects, however, associations with risk factors were weak or nonexistent, and two (obesity and total cholesterol) were inverse. Neither of these relations remained in multivariate analysis and thus may have been confounded by other factors.

Failure to find an association between ventricular arrhythmias and hypertension has been reported previously (1,2) but is somewhat surprising given the strong associations in the present study with increased left ventricular mass and measures of impaired left ventricular function. Although these measures of subclinical disease could have been related to previous hypertension, our definition of hypertension included past diagnoses, and only 9% of CHS subjects with a history of hypertension failed to meet blood pressure or medication criteria at examination.

The strong associations between bradycardia/conduction blocks and insulin, fibrinogen and Factor VII are interesting but defy biologic explanations at present. To our knowledge, no relation has yet been established between coagulation factors and bradycardia/conduction blocks, despite their strong independent relations in multivariate analysis. The relations found in the current study, although intriguing, should be considered only as a basis for future hypothesis generation and testing.

Conclusions. Ambulatory ECG monitoring revealed ventricular arrhythmias (excluding ectopic beats <15/h) in 16% of women and 28% of men in this population-based sample of community-dwelling older adults. Supraventricular arrhythmias were detected in more than half of all subjects and increased in frequency with increasing age. Bradycardia and conduction blocks were rare and were unassociated with age. Although ventricular arrhythmias were related to previous cardiovascular disease and measures of subclinical disease, such associations for the most part were not detected for supraventricular arrhythmias and bradycardia/conduction blocks. Associations with cardiovascular disease and its risk factors differed strongly by gender. Although risk related to arrhythmias can only be determined by prospective study, such studies should have adequate power in women and men to examine potential gender differences in associations.

Appendix

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